~~SH~~ Schultz 09/700906

FILE 'REGISTRY' ENTERED AT 15:26:58 ON 20 AUG 2002
L1 4 SEA FILE=REGISTRY ABB=ON PLU=ON ACCAGGCGTCTCGTGGGCCACAT /SQSN
L3 3 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=<50

L3 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 390223-46-8 REGISTRY
CN GenBank AX009578 (9CI) (CA INDEX NAME)
CI MAN
SQL **23**

SEQ 1 accaggcgtc tcgtgggcca cat
========== ========== ===
HITS AT: 1-23

L3 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 251353-35-2 REGISTRY
CN 2: PN: DE19822954 PAGE: 3 unclaimed DNA (9CI) (CA INDEX NAME)
CI MAN
SQL **23**

SEQ 1 accaggcgtc tcgtgggcca cat
========== ========== ===
HITS AT: 1-23

REFERENCE 1: 132:9597

L3 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 251301-36-7 REGISTRY
CN DNA, d(P-thio)(A-C-C-A-G-G-C-G-T-C-T-C-G-T-G-G-G-C-C-A-C-A-T) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: DE19822954 SEQID: 3 claimed DNA
CI MAN
SQL **23**

SEQ 1 accaggcgtc tcgtgggcca cat
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HITS AT: 1-23

REFERENCE 1: 132:9597

FILE 'HCAPLUS' ENTERED AT 15:27:27 ON 20 AUG 2002
L4 1 S L3

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:761162 HCAPLUS
DOCUMENT NUMBER: 132:9597
TITLE: Antisense oligonucleotides directed to cell cycle-associated protein Ki-67 mRNA for killing proliferating cells
INVENTOR(S): Flad, Hans-Dieter; Gerdes, Johannes; Boehle, Andreas; Deinert, Irina
PATENT ASSIGNEE(S): Forschungszentrum Borstel Zentrum fuer Medizin und Biowissenschaften, Germany
SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19822954	A1	19991125	DE 1998-19822954	19980522
WO 9961607	A2	19991202	WO 1999-EP3451	19990520
WO 9961607	A3	20000323		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9943636	A1	19991213	AU 1999-43636	19990520
EP 1080192	A2	20010307	EP 1999-926337	19990520

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: DE 1998-19822954 A 19980522
WO 1999-EP3451 W 19990520

AB Use of antisense oligonucleotides to Ki-67 mRNA to kill proliferating cells is disclosed. The cytotoxic effects on bladder carcinoma cells of a 23-base oligodeoxyribonucleotide complementary to Ki-67 mRNA encoding the N-terminus was demonstrated.

IT **251301-36-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antisense oligonucleotide; antisense oligonucleotides directed to cell cycle-assocd. protein Ki-67 mRNA for killing proliferating cells)

IT **251353-35-2**, 2: PN: DE19822954 PAGE: 3 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; antisense oligonucleotides directed to cell cycle-assocd. protein Ki-67 mRNA for killing proliferating cells)

=> fil hom

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NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 27	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28	Oct 21	EVENTLINE has been reloaded
NEWS 29	Oct 24	BEILSTEIN adds new search fields
NEWS 30	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 32	Nov 18	DKILIT has been renamed APOLLIT
NEWS 33	Nov 25	More calculated properties added to REGISTRY
NEWS 34	Dec 02	TIBKAT will be removed from STN

NEWS EXPRESS	October 14 CURRENT WINDOWS VERSION IS V6.01, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 16:07:17 ON 03 DEC 2002

=> FIL MEDLINE BIOSIS SCISEARCH CA
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FULL ESTIMATED COST	1.26	1.26

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=> s ki-67 or ki!67 or (ki 67) or (ki (n) 67)
L1 16593 KI-67 OR KI!67 OR (KI 67) OR (KI (N) 67)

=> s antisense or (complemen? (2n) ((nucl? (2n) acid) or oligo?)))
UNMATCHED RIGHT PARENTHESIS 'OLIGO?)))'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> s antisense or (complemen? (2n) ((nucl? (2n) acid) or oligo?))
L2 89425 ANTISENSE OR (COMPLEMEN? (2N) ((NUCL? (2N) ACID) OR OLIGO?))

=> s l1 and l2
L3 67 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 35 DUP REM L3 (32 DUPLICATES REMOVED)

=> s l4 and py=<1999
.2 FILES SEARCHED...
L5 15 L4 AND PY=<1999

=> d l5 1-15 ibib abs

L5 ANSWER 1 OF 15 MEDLINE
ACCESSION NUMBER: 1999299869 MEDLINE
DOCUMENT NUMBER: 99299869 PubMed ID: 10372654
TITLE: Complex regulation of prothymosin alpha in mammary tumors arising arising in transgenic mice.
AUTHOR: Loidi L; Garcia-Caballero T; Vidal A; Zalvide J; Gallego R; Dominguez F

CORPORATE SOURCE: Departamento de Fisiologia, School of Medicine, Universidad de Santiago de Compostela, Spain.
SOURCE: LIFE SCIENCES, **(1999)** 64 (23) 2125-33.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 20000303
Entered Medline: 19990625

AB Expression of prothymosin alpha (PTA) has been related to cell proliferation, both normal and pathological. PTA has also been proposed to be a target of the c-myc protooncogene. To study PTA mRNA levels during pathological cell growth, and especially the effect of the activation of specific oncogenes on PTA expression, we have studied its expression in tumors that arise in transgenic mice. We found high PTA levels in mammary tumors arising in c-myc, c-neu, and v-ras transgenic mice. Levels of this protein were variable between different tumors, and there is a differential regulation of PTA respect to other putative c-myc target genes, such as Ornithine Decarboxylase (ODC). Furthermore, expression of PTA is not absolutely dependent of c-myc expression, as shown by MYC depletion experiments performed with **antisense** oligonucleotides. We conclude that regulation of PTA in these tumors is complex and depends on more than a single activated oncogene.

L5 ANSWER 2 OF 15 MEDLINE
ACCESSION NUMBER: 1999038611 MEDLINE
DOCUMENT NUMBER: 99038611 PubMed ID: 9821170
TITLE: **Antisense** epidermal growth factor receptor RNA transfection in human malignant glioma cells leads to inhibition of proliferation and induction of differentiation.
AUTHOR: Tian X X; Lam P Y; Chen J; Pang J C; To S S; Di-Tomaso E; Ng H K
CORPORATE SOURCE: Department of Anatomical & Cellular Pathology, Prince of Wales Hospital, Chinese University of Hong Kong, Shatin, China.
SOURCE: NEUROPATHOLOGY AND APPLIED NEUROBIOLOGY, **(1998 Oct)** 24 (5) 389-96.
Journal code: 7609829. ISSN: 0305-1846.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990202
Last Updated on STN: 20000303
Entered Medline: 19990121

AB The epidermal growth factor receptor (EGFR) is a protooncogene that is frequently observed with alterations in late stage gliomas, suggesting an important role of this gene in glial tumorigenesis and progression. In this study we evaluated an **antisense** EGFR approach as an alternative therapeutic modality for glioblastomas. We transfected U-87MG cells with an **antisense** EGFR construct and obtained several clones stably expressing lower or undetectable levels of EGFR protein. These clones were found to have impaired proliferation as well as a reduced transforming potential to grow in soft agarose. The number of cells positive for the cell cycle-specific nuclear antigen **Ki-67** was also significantly decreased ($P < 0.05$) in **antisense** EGFR-transfected clones compared with parental or empty vector-transfected cells. Flow cytometric analysis revealed that the

proportion of cells in G0/G1 phases of the cell cycle in the **antisense** clones increased by up to 31% compared with control cells, whereas the proportion of cells in S phase decreased by up to 58%. In addition, the **antisense** EGFR-transfected cells showed higher expression of glial fibrillary acidic protein and a more differentiated form, with smaller cell bodies possessing fine tapering cell processes. These results suggest that EGFR plays a major role in modulating cell growth and differentiation in glioblastoma cells. Our experimental model of **antisense** EGFR provides a basis for future development of **antisense** EGFR oligodeoxynucleotides in treatment of glioblastomas.

L5 ANSWER 3 OF 15 MEDLINE
ACCESSION NUMBER: 97407638 MEDLINE
DOCUMENT NUMBER: 97407638 PubMed ID: 9264387
TITLE: POEMS syndrome: report on six patients with unusual clinical signs, elevated levels of cytokines, macrophage involvement and chromosomal aberrations of bone marrow plasma cells.
AUTHOR: Rose C; Zandecki M; Copin M C; Gosset P; Labalette M; Hatron P Y; Jauberteau M O; Devulder B; Bauters F; Facon T
CORPORATE SOURCE: Laboratoire d'Hematologie A, CHU, Lille, France.
SOURCE: LEUKEMIA, **(1997 Aug)** 11 (8) 1318-23.
Journal code: 8704895. ISSN: 0887-6924.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970916
Last Updated on STN: 19970916
Entered Medline: 19970904

AB POEMS syndrome is a multisystemic disorder characterized by the association of polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes and various other systemic clinical signs. The pathophysiology of this syndrome remains largely unknown. In order to gain insight into its pathophysiology, we studied the clinical characteristics and performed serum analysis (auto-antibodies, cytokine levels) and phenotypic and cytogenetic studies of bone marrow plasma cells (BMPC) in six patients with unequivocal POEMS syndrome. Two unusual clinical signs were present in these patients: pulmonary hypertension (two patients) and diffuse cutaneous necrosis (one patient). No auto-antibodies against peripheral nerve (PN) antigens (SGPG and SGLPG glycolipids, GM1, GD1a, GD1b and GT1b gangliosides) were found. Sequential evaluations of serum cytokines (IL-1-beta, IL-6 and TNF-alpha) showed a moderate to marked elevations of IL-6 and TNF-alpha in all patients (up to six-fold for TNF-alpha and 16-fold for IL-6). Using in situ hybridization of these cytokines mRNAs on lymph node specimens of two patients who had an angiofollicular lymph node hyperplasia, a strong positivity was found with the IL-1-beta **antisense** probe in lymph node macrophages. On skin biopsy a high number of cells expressing TNF-alpha mRNA was observed in the dermis. The biological features of BMPC: phenotype (expression of CD19 and CD56 antigens), kinetics (**Ki-67** index), karyotype, DNA content and chromosomal in situ hybridization remained those of BMPC found in monoclonal gammopathy of undetermined significance. We conclude that POEMS syndrome is a hypercytokinemic syndrome in which BMPC are not of malignant type. Macrophages are involved in this syndrome and their role has to be further investigated as well as treatments which act through an anti-cytokine mechanism.

L5 ANSWER 4 OF 15 MEDLINE
ACCESSION NUMBER: 97073235 MEDLINE
DOCUMENT NUMBER: 97073235 PubMed ID: 8915983

TITLE: **Antisense** oligonucleotides to proliferating cell nuclear antigen and **Ki-67** inhibit human mesangial cell proliferation.
AUTHOR: Maeshima Y; Kashihara N; Sugiyama H; Makino H; Ota Z
CORPORATE SOURCE: Third Department of Internal Medicine, Okayama University Medical School, Japan.
SOURCE: JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, **(1996 Oct)** 7 (10) 2219-29.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970226

AB Proliferating cell nuclear antigen (PCNA) and **Ki-67** are cell cycle-associated nuclear proteins and are used as markers for proliferating cells. This study attempted to inhibit glomerular mesangial cell (MC) proliferation, which is the hallmark of many forms of glomerular disease, by inhibiting these nuclear proteins with **antisense** oligodeoxynucleotides. The **antisense** and sense phosphorothioate **oligodeoxynucleotides complementary** to PCNA and **Ki-67** mRNA, including the initiation codon, were synthesized. Human MC were cultured in growth medium in the presence of sense or **antisense** oligodeoxynucleotides, and the effects of these oligodeoxynucleotides on mesangial cell proliferation were evaluated by direct cell count. Both PCNA and **Ki-67** **antisense** oligodeoxynucleotides significantly inhibited mesangial cell proliferation as compared with sense oligodeoxynucleotides. **Antisense** oligodeoxynucleotides (10 microM) for PCNA and **Ki-67** inhibited mesangial cell growth by greater than 50%. The effect of **antisense** oligodeoxynucleotides on target protein expression was examined by immunocytochemistry using specific monoclonal antibodies. Reverse transcription-polymerase chain reaction also was performed to evaluate the effect of **antisense** oligodeoxynucleotides on PCNA and **Ki-67** mRNA expression. Studies of target protein and mRNA expression revealed that the inhibitory effects of the **antisense** oligonucleotides were mediated through decreases in the expression of both mRNA and protein. Sense oligodeoxynucleotides produced little effect. These results indicate that **antisense** oligodeoxynucleotides targeting PCNA and **Ki-67** mRNA reduce the expression of these gene products and inhibit mesangial cell proliferation. Moreover, these results suggest the feasibility of **antisense** strategies designed to inhibit PCNA and **Ki-67** expression for the inhibition of mesangial cell proliferation in vivo.

L5 ANSWER 5 OF 15 MEDLINE
ACCESSION NUMBER: 96323428 MEDLINE
DOCUMENT NUMBER: 96323428 PubMed ID: 8744726
TITLE: Cell proliferation-associated nuclear antigen defined by antibody **Ki-67**: a new kind of cell cycle-maintaining proteins.
AUTHOR: Duchrow M; Schluter C; Key G; Kubbutat M H; Wohlenberg C; Flad H D; Gerdes J
CORPORATE SOURCE: Department of Immunology and Cell Biology, Forschungsinstitut Borstel, Germany.
SOURCE: ARCHIVUM IMMUNOLOGIAE ET THERAPIAE EXPERIMENTALIS, **(1995)** 43 (2) 117-21. Ref: 30
Journal code: 0114365. ISSN: 0004-069X.
PUB. COUNTRY: Poland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961025
Last Updated on STN: 19961025
Entered Medline: 19961016

AB A decade of studies on the human nuclear antigen defined by monoclonal antibody **Ki-67** (the "**Ki-67** protein") has made it abundantly clear that this structure is strictly associated with human cell proliferation and that the expression of this protein can be used to assess the growth fraction of a given cell population. Until recently the **Ki-67** protein was described as a nonhistone protein that is highly susceptible to protease treatment. We have isolated and sequenced cDNAs encoding for this antigen and found two isoforms of the full length cDNA of 11.5 and 12.5 kb, respectively, sequence and structure of which are thus far unique. The gene encoding the **Ki-67** protein is organized in 15 exons and is localized on chromosome 10. The center of this gene is formed by an extraordinary 6845 bp exon containing 16 successively repeated homologous segments of 366 bp ("**Ki-67** repeats"), each containing a highly conserved new motif of 66 bp ("**Ki-67** motif"). The deduced peptide sequence of this central exon possess 10 ProGluSerThr (PEST) motifs which are associated with high turnover proteins such as other cell cycle-related proteins, oncogenes and transcription factors, etc. Like the latter proteins the **Ki-67** antigen plays a pivotal role in maintaining cell proliferation because **Ki-67** protein **antisense** oligonucleotides significantly inhibit 3H-thymidine incorporation in permanent human tumor cell lines in a dose-dependent manner.

L5 ANSWER 6 OF 15 MEDLINE
ACCESSION NUMBER: 95293600 MEDLINE
DOCUMENT NUMBER: 95293600 PubMed ID: 7775120
TITLE: Modulation of cellular functions in retroorbital fibroblasts using **antisense** oligonucleotides targeting the c-myc protooncogene.
AUTHOR: Heufelder A E; Bahn R S
CORPORATE SOURCE: Molecular Thyroid Research Laboratory, Ludwig-Maximilians Universitat, Munchen, Germany.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, **(1995 Jun)** 36 (7) 1420-32.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950720
Last Updated on STN: 19970203
Entered Medline: 19950710

AB PURPOSE. To examine the signal transduction pathways involved in the activation of orbital fibroblast effector functions relevant to the pathogenesis of Graves' ophthalmopathy (GO). To determine, using **antisense** technology, whether the c-myc protooncogene is involved in cell proliferation and glycosaminoglycan (GAG) synthesis in cultured orbital fibroblasts (OF). METHODS. The effects of a 16-mer c-myc **antisense** phosphorothioate oligodeoxynucleotide (S-ODN) on OF monolayers derived from orbital connective tissue of patients with severe GO (n = 6) and healthy individuals (n = 3) were investigated. Quiescent OF monolayers were treated with serum or cytokines and were exposed to

increasing concentrations of a c-myc **antisense** S-ODN and several control S-ODN. Cell proliferation was quantitated by direct cell counting and by immunocytochemistry for the nuclear **Ki-67** antigen. Glycosaminoglycan synthesis was examined by [3H] GAG analysis. The effects of the c-myc **antisense** S-ODN and control S-ODN on c-myc mRNA and protein product levels were analyzed using reverse-transcriptase polymerase chain reaction, immunocytochemistry, and immunoblotting, respectively. RESULTS. Transient suppression of c-myc mRNA and the c-myc protein product by a c-myc **antisense** S-ODN (2 to 8 microM) strongly inhibited cell proliferation and GAG synthesis in OF derived from patients with GO and healthy individuals. These effects occurred in a dose-dependent manner and were specific for the c-myc **antisense** S-ODN used. Cell morphology or viability were not affected. CONCLUSIONS. The c-myc protooncogene and its protein product are involved in the proliferative and metabolic activities of OF exposed to serum or cytokines in vitro. C-myc appears to be an essential component of at least two OF cellular activities likely to contribute to the orbital tissue alterations in GO.

L5 ANSWER 7 OF 15 MEDLINE
ACCESSION NUMBER: 95234542 MEDLINE
DOCUMENT NUMBER: 95234542 PubMed ID: 7718451
TITLE: Use of in situ detection of histone mRNA in the assessment of epidermal proliferation: comparison with the Ki67 antigen and BrdU incorporation.
AUTHOR: Smith M D; Healy E; Thompson V; Morley A; Rees J L
CORPORATE SOURCE: Department of Dermatology, University of Newcastle upon Tyne, Royal Victoria Infirmary, U.K.
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, **(1995 Mar)** 132 (3) 359-66.
Journal code: 0004041. ISSN: 0007-0963.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950605
Last Updated on STN: 19950605
Entered Medline: 19950524

AB The labelling index is commonly used as a measure of proliferation. However, the use of tritiated thymidine or BrdU labelling of S-phase cells is limited to prospective samples. We have employed an **oligonucleotide** cocktail **complementary** to the mRNA species encoding the replication-dependent histones H2B, H3 and H4 for non-isotopic in situ hybridization (NISH), and have compared the resultant proliferation indices in normal skin with those obtained by bromodeoxyuridine (BrdU) incorporation and by Ki67 immunohistochemistry (IHC) using the monoclonal antibody MIB1. In addition, we compared the staining characteristics of histone NISH and Ki67 IHC in a further 25 samples from a variety of inflammatory dermatoses and neoplastic conditions, as well as from normal skin. In normal skin, S-phase (histone NISH and BrdU) and cycling (Ki67) cells were confined to the basal and low suprabasal layers. The labelling indices determined by histone NISH and BrdU incorporation were similar, whereas that of Ki67 IHC was four times greater. In biopsies from hyperproliferative dermatoses and dysplastic or malignant lesions, the number of histone NISH- and Ki67 IHC-positive cells was generally elevated; in accordance with the differential expression of these two markers during the cell cycle, MIB1 consistently gave higher results. The advantage of histone NISH over Ki67 IHC is that it is a marker of the same part of the cell cycle as BrdU incorporation. However, the combined use of both histone NISH and Ki67 IHC to measure two cell cycle parameters, namely S-phase and the number of cycling cells, allows more detailed retrospective study of epidermal proliferation than has been

possible previously.

L5 ANSWER 8 OF 15 MEDLINE
ACCESSION NUMBER: 94043435 MEDLINE
DOCUMENT NUMBER: 94043435 PubMed ID: 8227122
TITLE: The cell proliferation-associated antigen of antibody **Ki-67**: a very large, ubiquitous nuclear protein with numerous repeated elements, representing a new kind of cell cycle-maintaining proteins.
AUTHOR: Schluter C; Duchrow M; Wohlenberg C; Becker M H; Key G; Flad H D; Gerdes J
CORPORATE SOURCE: Department of Immunology and Cell Biology, Forschungsinstitut Borstel, Germany.
SOURCE: JOURNAL OF CELL BIOLOGY, **(1993 Nov)** 123 (3) 513-22.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X65550; GENBANK-X65551
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931207

AB The antigen defined by mAb **Ki-67** is a human nuclear protein the expression of which is strictly associated with cell proliferation and which is widely used in routine pathology as a "proliferation marker" to measure the growth fraction of cells in human tumors. **Ki-67** detects a double band with apparent molecular weights of 395 and 345 kD in immunoblots of proteins from proliferating cells. We cloned and sequenced the full length cDNA, identified two differentially spliced isoforms of mRNA with open reading frames of 9,768 and 8,688 bp encoding for this cell proliferation-associated protein with calculated molecular weights of 358,761 D and 319,508 D, respectively. New mAbs against a bacterially expressed part and a synthetic polypeptide deduced from the isolated cDNA react with the native **Ki-67** antigen, thus providing a circle of evidence that we have cloned the authentic **Ki-67** antigen cDNA. The central part of the **Ki-67** antigen cDNA contains a large 6,845-bp exon with 16 tandemly repeated 366-bp elements, the "**Ki-67** repeats", each including a highly conserved new motif of 66 bp, the "**Ki-67** motif", which encodes for the epitope detected by **Ki-67**. Computer analysis of the nucleic acid and the deduced amino acid sequence of the **Ki-67** antigen confirmed that the cDNA encodes for a nuclear and short-lived protein without any significant homology to known sequences. **Ki-67** antigen-specific **antisense** oligonucleotides inhibit the proliferation of IM-9 cell line cells, indicating that the **Ki-67** antigen may be an absolute requirement for maintaining cell proliferation. We conclude that the **Ki-67** antigen defines a new category of cell cycle-associated nuclear nonhistone proteins.

L5 ANSWER 9 OF 15 MEDLINE
ACCESSION NUMBER: 94006251 MEDLINE
DOCUMENT NUMBER: 94006251 PubMed ID: 8402644
TITLE: p53 mutations and histological type of invasive breast carcinoma.
AUTHOR: Marchetti A; Buttitta F; Pellegrini S; Campani D; Diella F; Cecchetti D; Callahan R; Bistocchi M
CORPORATE SOURCE: Institute of Pathological Anatomy and Histology, University of Pisa, Italy.

SOURCE: CANCER RESEARCH, **(1993 Oct 1)** 53 (19) 4665-9.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931102

AB A polymerase chain reaction-single strand conformation polymorphism assay was used to assess p53 mutations in 148 invasive breast carcinomas, selected on the basis of their histotype. They comprised 56 lobular, 47 ductal, 19 mucinous, 18 medullary, and 8 papillary carcinomas. The distribution of p53 mutations was significantly different (P = 0.006) in the histotypes examined: mutations were frequent in medullary (39%) and ductal (26%), less common in lobular (12%), and absent in mucinous and papillary carcinomas. The frequency of mutations in the exon 5 of the p53 gene was significantly higher in medullary carcinomas than in the other histotypes: 5 (63%) of the mutations found in exon 5 were observed in medullary carcinomas (P = 0.012). One hundred twenty-two tumors from the total were also examined by immunohistochemistry for p53 overexpression using antibody PAb 1801. A specific immunostaining in neoplastic cells was present in 12 tumors. A strong correlation (P < 0.001) was observed between p53 mutations and nuclear accumulation of the p53 protein: 10 tumors were scored positive for both p53 mutation and overexpression. However, in 9 cases having a mutated p53 gene we failed to find a positive immunoreaction. A significant association (P = 0.01) was present between mutations in the p53 gene and high proliferative activity of the tumors determined by immunohistochemistry with monoclonal antibody **Ki-67**. Moreover, a significantly higher expression of the **Ki-67** antigen was found in medullary carcinomas compared to the other histotypes. Our findings indicate that in invasive breast carcinomas structural abnormalities of the p53 gene are mainly seen in medullary and ductal tumors and that the other histological types, especially those associated with a high level of differentiation and favorable prognosis, show a very low incidence of p53 mutations.

L5 ANSWER 10 OF 15 MEDLINE
ACCESSION NUMBER: 91296868 MEDLINE
DOCUMENT NUMBER: 91296868 PubMed ID: 2068146
TITLE: **Antisense** inhibition of N-myc reduces cell growth but does not affect c-myc expression in the neuroepithelioma cell line CHP100.
AUTHOR: Rosolen A; Whitesell L; Ikegaki N; Kennett R; Neckers L M
CORPORATE SOURCE: Medicine Branch, NCI, National Institutes of Health, Bethesda, MD 20982.
SOURCE: PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, **(1991)** 366 29-36.
Journal code: 7605701. ISSN: 0361-7742.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910901
Last Updated on STN: 20000303
Entered Medline: 19910809

L5 ANSWER 11 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:518947 BIOSIS
DOCUMENT NUMBER: PREV199497531947
TITLE: Inhibition of human mesangial cell proliferation by

antisense oligonucleotide targeting proliferating cell nuclear antigen and **Ki-67** mRNA.

AUTHOR(S): Maeshima, Y.; Kashihara, N.; Sugiyama, H.; Sekikawa, T.; Okamoto, K.; Kanao, K.; Morita, Y.; Yamasaki, Y.; Makino, H.; Ota, Z.

CORPORATE SOURCE: Okayama Univ. Med. Sch., Okayama Japan

SOURCE: Journal of the American Society of Nephrology, (1994) Vol. 5, No. 3, pp. 786.
Meeting Info.: Abstracts Submitted for the 27th Annual Meeting of the American Society of Nephrology Orlando, Florida, USA October 26-29, 1994
ISSN: 1046-6673.

DOCUMENT TYPE: Conference

LANGUAGE: English

L5 ANSWER 12 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 94:615335 SCISEARCH

THE GENUINE ARTICLE: PG771

TITLE: INHIBITION OF HUMAN MESANGIAL CELL-PROLIFERATION BY **ANTISENSE** OLIGONUCLEOTIDE TARGETING PROLIFERATING CELL NUCLEAR ANTIGEN AND **KI-67** MESSENGER-RNA

AUTHOR: MAESHIMA Y (Reprint); KASHIHARA N; SUGIYAMA H; SEKIKAWA T; OKAMOTO K; KANAO K; MORITA Y; YAMASAKI Y; MAKINO H; OTA Z

CORPORATE SOURCE: OKAYAMA UNIV, SCH MED, OKAYAMA 700, JAPAN

COUNTRY OF AUTHOR: JAPAN

SOURCE: JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (**SEP 1994**) Vol. 5, No. 3, pp. 786.
ISSN: 1046-6673.

DOCUMENT TYPE: Conference; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: ENGLISH

REFERENCE COUNT: No References

L5 ANSWER 13 OF 15 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 132:9597 CA

TITLE: **Antisense** oligonucleotides directed to cell cycle-associated protein **Ki-67** mRNA for killing proliferating cells

INVENTOR(S): Flad, Hans-Dieter; Gerdes, Johannes; Boehle, Andreas; Deinert, Irina

PATENT ASSIGNEE(S): Forschungszentrum Borstel Zentrum fuer Medizin und Biowissenschaften, Germany

SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19822954	A1	19991125	DE 1998-19822954	19980522 <--
WO 9961607	A2	19991202	WO 1999-EP3451	19990520 <--
WO 9961607	A3	20000323		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9943636	A1	19991213	AU 1999-43636	19990520 <--
EP 1080192	A2	20010307	EP 1999-926337	19990520

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: DE 1998-19822954 A 19980522
WO 1999-EP3451 W 19990520

AB Use of **antisense** oligonucleotides to **Ki-67** mRNA to kill proliferating cells is disclosed. The cytotoxic effects on bladder carcinoma cells of a 23-base **oligodeoxyribonucleotide complementary** to **Ki-67** mRNA encoding the N-terminus was demonstrated.

L5 ANSWER 14 OF 15 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 131:253340 CA
TITLE: Characterization of mRNA patterns in neurons and single cells for medical diagnosis and therapeutics
INVENTOR(S): Eberwine, James; Dichter, Marc; Miyashiro, Kevin
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: U.S., 20 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5958688	A	19990928	US 1997-848131	19970428 <--

AB A method of identifying neurite cDNA clones by detg. and comparing mRNA expression in selected neurites is provided. Complementary DNA clones identified by this method are also provided. In addn., methods of profiling mRNA expression and diagnosing and treating conditions assocd. with a pattern of mRNA expression by detg. an mRNA expression profile in selected cells are provided.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 15 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 131:39728 CA
TITLE: Agent for gene therapy of tumors and neurodegenerative, cardiovascular, and autoimmune diseases
INVENTOR(S): Reszka, Regina; Berndt, Antje
PATENT ASSIGNEE(S): Max-Delbrueck-Centrum fuer Molekulare Medizin, Germany
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930741	A2	19990624	WO 1998-DE3763	19981214 <--
WO 9930741	A3	19990819		

W: JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

DE 19859526	A1	19990819	DE 1998-19859526	19981214 <--
EP 1037670	A2	20000927	EP 1998-966568	19981214

R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE, FI

JP 2002508337	T2	20020319	JP 2000-538719	19981214

PRIORITY APPLN. INFO.: DE 1997-19756309 A 19971212
WO 1998-DE3763 W 19981214

AB A method for local/regional gene therapy of tumors (esp. liver metastases) and of neurodegenerative, cardiovascular, and autoimmune diseases comprises combined application of liposomes/plasmid DNA complexes having different compns., quantities, and concns. The pharmaceutical agent employed comprises .gtoreq.1 genetic material which are nonencapsulated or encapsulated in PEG, immuno-, immuno/PEG, or cationic, optionally polymer-modified liposomes; lyophilized or degradable starch particles and/or gelatin and/or polymer nanoparticles; and a contrast agent contg. I, Gd, magnetite, or F. The genetic material preferably constitutes a suicide gene such as herpes simplex virus thymidine kinase (HSV-tk) gene, deaminase gene, or a cytokine gene coding for IL-2, IL-4, IL-6, IL-10, IL-12, or IL-15, and is enclosed in multilamellar liposomes comprising an amphiphile, a steroid, and an anionic lipid. Thus, phosphatidylcholine-cholesterol-PEG liposomes contg. suicide gene pUT 649, which encodes HSV-tk, were injected together with a drug carrier embolization system into the common hepatic artery of rats which had been inoculated with CC531 carcinoma cells 10 days previously. Beginning 5 days later, the rats were treated with ganciclovir (100 mg/kg/day i.p.) for 14 days. The rats showed a decrease in liver metastases after 30 days owing to conversion of ganciclovir by HSV-tk to a nucleotide-like compd. which was incorporated into the DNA of dividing liver cells, causing cessation of DNA synthesis.

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	45.67	46.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.77	-1.77

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